10 Timing of Appendectomy for Acute Appendicitis: Can Surgery Wait?

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Case Example

A 9-year-old boy presents at 10 PM with right lower quadrant abdominal pain and undergoes an ultrasound confirming appendicitis. The on-call surgeon prefers to perform the appendectomy immediately with concern that delay may lead to perforation. The anesthesiologist on call challenges the need for immediate surgery and remarks that the cost of bringing in an operative team in the middle of the night is not justified from either a fiscal or "standard of care" perspective. After further debate, they agree to book the case for 6:30 AM the following morning before electively scheduled cases begin.

Introduction

The scenario described above is likely to be quite common; controversy and lack of consensus around the safety and fiscal implications of delaying appendectomy until the following morning exist even among pediatric surgeons. The published literature would suggest a growing trend toward acceptance of operative delay (at least until the following day for patients presenting the night before), but is this justified by the available evidence? What is the impact of time to appendectomy (TTA) following hospital presentation on the risk of appendiceal perforation and postoperative complications? How does delay of appendectomy impact resource

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utilization and hospital cost? Several studies have attempted to shed light on these questions using a wide variety of analytic methods, some with conflicting results. The goal of this review was to provide a critical review of the available literature to shed light on the influence of treatment delay on both clinical and fiscal outcomes. Specifically, we wished to explore this relationship in the context of three categories: (1) risk of complicated or perforated appendicitis found at operative exploration, (2) risk of adverse events in the postoperative period, and (3) resource utilization, including hospital cost, length of hospital stay, and readmission.

Literature Review

Literature searches were performed in English using Medline, PubMed, and pertinent Cochrane reviews. A comprehensive literature search was conducted using the following search terms: appendicitis, appendectomy, timeliness, delay, timing of surgery, perforation, and complicated appendicitis. All identified studies were manually reviewed for outcomes of interest rather than using additional search terms to be comprehensive. Further cross-checking was performed by reviewing the reference list associated with all studies included in the reference list of this review.

For the purpose of this review, only studies exclusively reporting on outcomes in patients 18 years of age and younger were included. This decision was based on the evidence-based premise that “children are not small adults” with respect to factors that may impact the measurable association between treatment delay and outcomes. These include factors influencing timelines of presentation, disease progression, and rate of perforation at hospital presentation. Furthermore, it was the opinion of the author that the current pool of pediatric evidence was of sufficient volume and rigor to stand alone without the need to include adult-specific data (which could compromise both generalizability and external validity).

Studies that reported outcomes associated with treatment delay in calendar days rather than hours were also excluded. This was done to focus the review on studies that were calibrated to address the contemporary clinical question as to whether a modest delay in appendectomy (i.e., the next morning for a patient presenting in the evening the night before) is a safe and fiscally reasonable practice. Studies reporting outcomes in calendar days (large database studies such as KID and NIS) are likely to misclassify many patients when attempting to address this clinical question. To illustrate further, a patient who presents at 11:30 PM and then undergoes an appendectomy 2 hours later at 1:30 AM the next calendar day would be categorized as a “next day” (2 calendar days) appendectomy, while a patient who presents at 12:30 AM and then undergoes appendectomy 20 hours later at 8:30 PM would be considered a “same day” (1 calendar day) appendectomy. Such misclassification will bias the analysis toward the null hypothesis (no difference between same day and next day appendectomy) even if an increased risk of adverse outcomes actually exists.

Discussion

Treatment Delay and Risk of Perforated Disease

Nine studies were identified that explored an association between timing of appendectomy and risk of complicated or perforated appendicitis. Collectively, these studies included 8473 patients from 42 different hospitals. Seven (78%) of studies were retrospective and five (56%) were single-center experiences (Table 10.1).

Overall, seven (78%) of the nine studies did not find an association between delay and risk of perforation or complicated appendicitis. However, it should be noted that the available literature pool was quite heterogeneous with respect to analytic methods and definitions for both exposures and outcomes. These included a lack of standardized definitions for assessing perforation and complicated disease, as well as differences between studies in measuring time from presentation or admission to appendectomy. A formal meta-analysis to aggregate data across studies was therefore not possible.

Given the heterogeneity of available data, a critical review of the potential sources of bias associated with different study designs and analytic methods is important to gauge the strength of different studies. In this regard, two studies in the review were identified as prospective cohort designs. Based on the relatively well-documented and objective nature of ED presentation and surgical start time (exposure components), prospective study designs are not likely to provide more accurate TTA estimates compared to their retrospective counterparts. Furthermore, none of these studies specifically indicated how their prospective methodology improved the capture and accuracy of outcomes data (status of perforation or complicated appendicitis) from pathology and operative reports. Given these considerations, prospective studies should not be considered superior in their validity to retrospective study designs in this review.

The influence of clinical disease severity on timing of appendectomy is a potentially important source of bias and one that may greatly vary across hospitals. It is well established that most perforations in children occur prior to hospital presentation, and patients who are perforated on presentation typically have more severe clinical presentations compared to those who are not. Some hospitals may treat children with more severe presentations more expeditiously, while others may elect to obtain additional cross-sectional imaging or proceed with a period of resuscitation prior to appendectomy. Depending on a hospital's diagnostic and treatment approach, children who are perforated at time of presentation may have different TTA profiles at baseline compared to those who are not. This effect could bias the analyses between TTA and perforated disease in either direction. Early operative management of children with a pre-existing perforation would bias the analysis away from an association between TTA and perforation (even if one actually exists), while delayed operative intervention for pre-existing perforations may bias the analyses toward an association (even if one didn't exist). The former effect (early management of more severe disease) may explain why some studies have demonstrated a trend toward lower perforation rates with longer TTA (e.g., a "protective" effect with delay) [1].

Table 10.1 Summary of published studies reporting the association between timing of appendectomy and outcomes in the pediatric age group

					Outcomes associated with delay (main results)		
Citations	Study timeline (N)	Study design	Analytic method/ exposure groups	Outcomes definitions/criteria	Perforation	Adverse events	Resource utilization
Serres et al. [11]	2012–2014 (2116)	Multicenter retrospective cohort (16 hospitals)	Multivariable regression (exposure analyzed in quartiles of TTA)	Standardized cost (each billed item recalculated using the median cost from all 16 hospitals)	N/A	N/A	*Increased resource utilization found*; the longest quartile of TTA was associated with 23% higher total cost ($1589/case, RR:1.23, 95%CI:1.14–1.32, $p < 0.001$) and 53% higher room-associated cost ($906/case,RR:1.53, 95%CI:1.35–1.74, $p < 0.001$) compared to the shortest quartile
Serres et al. [10]	2012–2014 (2429)	Multicenter retrospective cohort (23 hospitals)	Multivariable regression (exposure analyzed in 1 hour increments); rates of complicated appendicitis also examined at each hospital (before/after their respective median TTAs)	Standardized NSQIP-Pediatric criteria used for complicated appendicitis (operative reports reviewed for free fecalith, abscess, diffuse fibropurulent exudate, visible hole) and all adverse event outcomes	*No increased risk found*; OR: 0.99 (95%CI:0.97–1.02) for each hour of delay in pooled analysis; no increased risk found for 22 of 23 hospitals when examined individually	*No increased risk found*; for each hour delay: SSI OR: 0.96 (95%CI:0.88–1.04), OSI OR: 1.00 (95%CI:0.95–1.05), drainage procedures OR: 1.02 (95%CI:0.97–1.07), unplanned reoperation OR: 1.00 (95%CI:0.93–1.07)	*No increased risk for readmissions*; OR: 1.01 (95%CI:0.99–1.04) for each hour of delay; *increased LOS found:* 0.06 days of increased LOS for each hour of treatment delay (95%CI:0.03–0.08 days)

Stevenson et al. [4]	Not reported (955)	Multicenter retrospective cohort (10 hospitals)	Multivariable regression (exposure analyzed in 1 hour increments)	Review of operative reports using standardized criteria for complicated appendicitis developed by study consortium (operative reports reviewed for perforation, rupture, complex appendicitis, purulent material, abscess)	*No increased risk found*; OR for all patients: 1.00 (95%CI:0.96–1.05) for each hour of delay, OR for subgroup analyses of longer delays between 12 and 24 hours, 0.93 (95%CI:0.79–1.08) for each hour of delay	N/A	N/A
Almstrom et al. [1]	2006–2013 (2756)	Single-center retrospective cohort	Multivariable regression (exposures groups: <12 vs. 12–24 hours)	Pathology and operative reports (operative reports reviewed for visible hole, purulent peritonitis, abscess)	*No increased risk found*; OR for delayed group: 0.79 (95%CI:0.87–1.36)	*No increased risk found*; SSI OR: 0.69 (95%CI:0.35–1.36), OSI OR: 0.76 (95%CI:0.48–1.20), reoperation OR: 1.13 (95%CI:0.41–3.16)	*No increased utilization found*; readmission OR: 0.79 (95%CI:0.49–1.26)

(continued)

Table 10.1 (continued)

					Outcomes associated with delay (main results)		
Citations	Study timeline (N)	Study design	Analytic method/ exposure groups	Outcomes definitions/criteria	Perforation	Adverse events	Resource utilization
Boomer et al. [9]	2010–2012 (1388)	Multicenter retrospective cohort (6 hospitals)	Multivariable regression and Cochran-Armitage test for trend using SSI as outcome. Complicated and uncomplicated appendicitis identified from operative reports and used for risk stratification, not for outcomes (exposures groups: <4 vs. 4–8 vs. 8–12 vs. 12–16 vs. >16 hours)	Standardized NSQIP-Pediatric criteria used for SSI outcomes; chart review used to categorize simple and complicated appendicitis for risk stratification	*No increased risk found*; *regression p-value* for delayed groups as both categorical and continuous variable >0.1 for both simple and complicated subgroups (no additional data provided)	*No increased risk found*; time not identified in multivariable regression as significant (OR data not provided in manuscript), SSI rates (<4 hours vs. >16 hours): 0.0 vs. 0.9% ($p = 0.58$) for simple appendicitis, 5.0 vs. 4.0% ($p = 1.0$) for complicated appendicitis	N/A
Meltzer et al. [3]	1998–2014 (857)	Multicenter retrospective cohort (5 hospitals)	Multivariable regression (exposures groups: <3 vs. 3–6 vs. >6 hours)	Operative reports (no further detail provided)	*Increased risk found*; OR for delayed group: 1.02 (95%CI:1.00–1.04) for each hour of delay	N/A	N/A

Gurien et al. [13]	2009–2012 (484)	Single-center retrospective cohort	Multivariable regression for perforation (exposure group: <16 vs. >16 hours); chi-square tests for adverse event analyses	Pathology reports; perforated appendicitis as diagnosed by preoperative imaging excluded	*No increased risk found*; OR for delayed group: 1.0 (95%CI:0.96–1.04)	*No increased risk found*; SSI OR: 0.69 (95%CI:0.35–1.36), OSI OR: 0.76 (95%CI:0.48–1.20), reoperation OR: 1.13 (95%CI:0.41–3.16)	N/A
Manderville et al. [14]	2002–2010 (230)	Single-center prospective cohort	Multivariable regression (exposures groups: <3 vs. 3–6 vs. >6 hours)	Pathology and operative reports (no further detail provided)	*No increased risk found*; OR for delayed groups: 0.81 (95%CI:0.35–1.88) for 4–6 hour group, 0.98 (95%CI:0.48–1.96)	N/A	*No increased utilization found*; no difference in median LOS or operative time found across groups
Bonadio et al. [2]	2004–2010 (248)	Single-center retrospective cohort	Multivariable regression (exposure groups: <8 vs. 8–16 vs. >16 hours)	Pathology and operative reports (operative reports reviewed for “diagnosis of perforation”)	*Increased risk found*; OR for delayed group: 2.05 (95%CI:1.00–3.10) for 8–16 hours, 4.22 (95%CI:3.17–5.27) for >16 hours; OR for all patients: 1.10 (95%CI:1.04–1.16) for each hour of delay	N/A	N/A

(continued)

Table 10.1 (continued)

					Outcomes associated with delay (main results)		
Citations	Study timeline (N)	Study design	Analytic method/ exposure groups	Outcomes definitions/criteria	Perforation	Adverse events	Resource utilization
Boomer et al. [12]	2010–2012 (1338)	Single-center retrospective cohort	Multivariable regression and Cochran-Armitage test for trend using SSI as outcome. Complicated and uncomplicated appendicitis identified from operative reports and used for risk stratification, not for outcomes (exposures groups: <4 vs. 4–8 vs. 8–12 vs. 12–16 vs. >16 hours)	Operative reports (to categorize simple and complicated appendicitis for risk stratification)	N/A	*No increased risk found*; time not identified in multivariable regression as significant (OR data not provided in manuscript), SSI rates (<4 hours vs. >16 hours): 2.4 vs. 1.5% ($p = 0.44$) for simple appendicitis, 11.1 vs. 15.2% ($p = 0.44$) for complicated appendicitis	N/A
Yardeni et al. [15]	1998–2001 (126)	Single-center retrospective cohort	Multivariable regression (exposures groups: <6 vs. 6–12 vs. >12 hours); chi-square tests used to compare proportions across groups for adverse events	Pathology reports (no further detail provided)	*No increased risk found*; regression p-value for delayed groups = 0.37 (no other data provided)	*No increased risk found*; OSI/drainage rates (<6 hours vs. >6 hours): 2.6 vs. 5.7% ($p = 0.067$), OSI/drainage rates (<6 hours vs. >6 hours): 2.6 vs. 5.7% ($p = 0.067$),	*Trend in increased utilization found for LOS*; <6 hours (1.7 days) vs. >6 hours (2.5 days), $p = 0.06$; *increased utilization found for median cost*; <6 hours ($7366) vs. >12 hours ($9893), $p = 0.02$

TTA time to appendectomy, *SSI* surgical site infection, *OSI* organ space infection, *LOS* length of stay, *OR* odds ratio, *CI* confidence interval

In an attempt to mitigate bias associated with unknown perforation status on presentation, several studies have reported using computed tomography (CT) to exclude patients with perforation suspected on imaging [2–4]. However, the lack of sensitivity for differentiating complicated from uncomplicated disease using cross-sectional imaging has been well documented in both the radiology and surgical literature [5–7]. Computed tomography may be quite sensitive for diagnosing late presentations with rim-enhancing fluid collections, although the far more common scenario is early perforation with a non-enhancing adjacent fluid collection and localized fat stranding. Gangrenous appendicitis without perforation is frequently encountered in these cases, and often times the radiology read is equivocal. Furthermore, the generalizability of results from these studies may be limited as patients undergoing CT scans are arguably a different cohort than those that undergo ultrasound only.

Many different approaches have been used for identifying and defining outcomes (perforated and complicated appendicitis). Use of histology alone can both over- and underestimate perforation rates depending on operative and pathology factors. Overestimation can occur from holes made in a gangrenous appendix during its removal, while underestimation may occur if only a small portion of the appendix is sectioned to confirm the diagnosis of appendicitis during pathology evaluation. Review of operative reports has been proposed as a more clinically relevant means to establish the presence of both perforation and complicated disease. In this regard, histological perforation has poorly defined correlates for adverse events and increased resource utilization, while the presence of certain intraoperative findings (e.g., abscess and extraluminal fecaliths) has well established associations with clinically relevant consequences (e.g., organ space infections and increased hospital cost) [8]. However, details regarding the criteria used to identify complicated appendicitis from operative reports were often poorly described and not standardized in most studies, with only four studies (all multicenter study designs) specifically describing efforts in their methodology to standardize and audit for the purpose of quality assurance [4, 9–11].

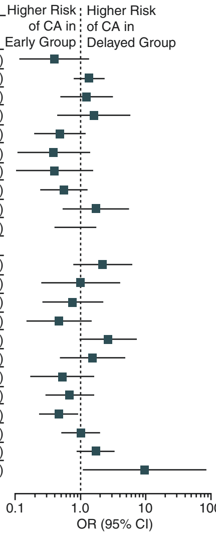
When considering the many different sources of potential bias described above, we would caution that the generalizability and external validity of any single-center experience may be greatly limited. A multicenter study design to balance out variation in disease severity-associated treatment delay coupled with a standardized methodology for assessing outcomes would provide the best possible analyses. Four studies included in this review included multicenter analyses, although two deserve special mention given their particularly wide scope and rigorous study designs. The first was a multicenter study of 955 patients from 10 hospitals which was sponsored by the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics [4]. The investigators used a broad definition of appendiceal perforation which included both the presence of a physical hole and indirect findings of perforation (e.g., abscess). Case definitions were defined a priori in a written manual of operations, and site investigators received detailed instruction on interpreting and coding of radiologic, operative, and pathology reports. Data quality checks were performed monthly with discrepant findings reviewed and corrected for the purpose of quality assurance. Following regression analyses adjusting for a wide variety of patient-level factors, the investigators found no increase in the risk of perforated appendicitis with increasing time from ED presentation to appendectomy. Furthermore, no association between TTA and perforated appendicitis was found in subgroup analyses of patients who were believed to be non-perforated based on CT obtained in the ED.

The second study included 2429 children undergoing appendectomy at 23 hospitals as part of a national collaborative supported by the American College of Surgeon's National Surgical Quality Improvement Program-Pediatric (NSQIP-Pediatric) [10]. The investigators utilized a definition for complicated disease that was developed and standardized through NSQIP's Data Definitions Committee and based on criteria associated with adverse outcomes and resource utilization. A standardized manual of operations and instructional webinar was created for study participants, and a clinical support network was established to ensure data collection integrity. Following regression analyses adjusting for a wide variety of patient-level factors, the investigators found no increase in the risk of complicated appendicitis with increasing time from ED presentation to appendectomy. It is notable that the results of this regression analysis using TTA as a continuous variable were remarkably similar to that from the emergency medicine collaborative study (OR for each hour of treatment delay: 1.00 [95%CI:0.96–1.05] vs. 0.99 [95%CI:0.97–1.02]). The investigators also performed a secondary analysis at the hospital level for each of the 23 participating hospitals. Comparison groups (early and late TTA) were defined by each hospital's median TTA. Exposures were defined in this manner to compare rates of complicated disease within a timeframe sensitive to each hospital infrastructure and diagnostic practices and to provide insight into whether a hospital could potentially reduce its rate of complicated disease by "shifting" patients from its late group to its early group. An increased risk of complicated appendicitis was found at only 1 of the 23 hospitals examined (Fig. 10.1). This finding suggests that internal efforts on behalf of individual hospitals to decrease their TTA (e.g., to improve the efficiency of the diagnostic process) would likely not lead to a reduction in their rate of complicated disease.

Treatment Delay and Risk of Adverse Events

Six studies reported outcomes associated with adverse events in the postoperative period. Several different types of adverse events were reported including surgical site infections (SSI), organ space infections (OSI), small bowel obstruction, percutaneous drainage procedures, and reoperation. Two studies used standardized NSQIP criteria for adverse event outcomes, while the remainder provided little detail around both definitions and efforts to standardize data collection and definitions. Issues surrounding heterogeneity of definitions and analytic bias were similar to that described above for perforation; however, it is noteworthy that none of the six studies examining adverse events found an association with treatment delay. These

	Median TTA, h			Complicated Appendicitis		
Hospital	Early Group	Late Group	Difference	Early Group	Late Group	OR (95% CI)
1	5	8.4	3.5	11/30	5/27	0.39 (0.12-1.33)
2	3.7	7.6	3.8	31/153	38/148	1.36 (0.79-2.33)
3	5.1	9.2	4	10/67	12/67	1.24 (0.50-3.11)
4	5.3	10.7	5.4	5/29	7/28	1.60 (0.44-5.80)
5	5.4	11.2	5.8	18/45	11/45	0.49 (0.20-1.20)
6	5.7	11.4	5.8	9/39	4/38	0.39 (0.11-1.41)
7	5.8	12	6.2	8/24	4/24	0.40 (0.10-1.57)
8	5.3	12.1	6.8	19/64	12/63	0.56 (0.24-1.27)
9	3.6	10.5	6.9	6/38	9/37	1.71 (0.54-5.42)
10	5.8	13.2	7.4	22/75	19/74	0.83 (0.41-1.71)
11	5.1	12.6	7.5	3/29	0/29	
12	4.4	11.9	7.5	6/73	12/73	2.20 (0.78-6.21)
13	5.2	13.1	7.9	5/24	5/24	1.00 (0.25-4.03)
14	4.8	13	8.2	9/56	7/55	0.76 (0.26-2.21)
15	5.5	13.8	8.3	11/35	6/34	0.47 (0.15-1.45)
16	5.4	13.8	8.4	7/48	15/48	2.66 (0.97-7.29)
17	4.6	13.6	9	11/24	13/23	1.54 (0.49-4.86)
18	7.1	16.4	9.3	14/25	10/25	0.52 (0.17-1.61)
19	5	14.5	9.5	18/48	14/48	0.69 (0.29-1.61)
20	5.5	15.1	9.6	30/85	17/84	0.47 (0.23-0.93)
21	5.1	15.2	10	20/111	20/110	1.01 (0.51-2.01)
22	6.9	17.9	11	22/79	31/78	1.71 (0.88-3.34)
23	10.3	21.5	11.1	1/23	7/23	9.63 (1.08-86.17)



A relative OR of 1 or less suggests a higher risk of CA in the early appendectomy group, whereas an OR greater than 1 suggests a higher risk of CA in the delayed appendectomy group. The relative OR of CA was indeterminate for hospital 11 because of a lack of patients with CA in the early time to appendectomy (TTA) group. Hospitals are ordered based on their relative rankings in the diffreneces in the median TTA of their early and late groups.

Fig. 10.1 Risk of complicated appendicitis associated with treatment delay at 23 children's hospitals. Hospitals are ordered from top to bottom by median time to appendectomy (TTA), and comparison groups (early and late TTA) were defined by each hospital's median TTA. Exposures were defined in this manner to compare rates of complicated disease within a timeframe sensitive to each hospital infrastructure and diagnostic practices and to provide insight into whether a hospital could potentially reduce its rate of complicated disease by decreasing its TTA relative to its median TTA. (Reproduced with permission from Serres et al. [10], Copyright© (2017) American Medical Association. All rights reserved)

included the two rigorous multicenter studies described above which also examined adverse event rates in addition to rates of complicated appendicitis [9, 10].

Treatment Delay and Impact on Resource Utilization

Five studies examined the association between treatment delay and resource utilization, including three reporting length of stay (LOS), two reporting readmission rates, and two reporting hospital cost. Two of the single-center studies examining LOS found either no association with treatment delay or a trend toward increased LOS. However, the number of patients included in these studies was relatively small which may have led to underpowered analyses. In a rigorously designed multicenter study of 2116 patients from 16 children's hospitals, Serres et al. found a 0.06-day increase in LOS associated with each hour of treatment delay [11]. Both studies examining hospital cost found an association with increased treatment delay, and these included the same study by Serres et al. which found a 23% difference in hospital cost between the longest and shortest quartiles of TTA (Table 10.2) [11]. None of the studies examining readmission rates found an association with readmission.

Table 10.2 Influence of time to appendectomy (categorized by hospital-specific quartiles) on hospital cost in 2116 patients at 16 children's hospitals

	Time to appendectomy				
	1st quartile	2nd quartile	3rd quartile	4th quartile	
Overall costs					
Adjusted mean	$6967	$7682	$7798	$8556	<0.001
Rate ratio (95% confidence intervals)	Ref	1.10 (1.03–1.18)	1.12 (1.04–1.2)	1.23 (1.14–1.32)	
Operating room costs					
Adjusted mean	$3739	$3930	$4084	$4005	<0.001
Rate ratio (95% confidence intervals)	Ref	1.05 (1.01–1.09)	1.09 (1.05–1.14)	1.07 (1.03–1.12)	
Operating room time-based costs					
Adjusted mean	$1400	$1360	$1370	$1332	0.22
Rate ratio (95% confidence intervals)	Ref	0.97 (093, 1.02)	0.98 (0.93, 1.03)	0.95 (0.91, 1.00)	
Operating room fixed costs					
Adjusted mean	$1912	$2188	$2266	$2305	<0.001
Rate ratio (95% confidence intervals)	Ref	1.14 (1.09, 1.2)	1.18 (1.12, 1.25)	1.21 (1.14, 1.27)	
Room costs					
Adjusted mean	$1695	$1723	$1853	$2601	<0.001
Rate ratio (95% confidence intervals)	Ref	1.01 (0.9–1.15)	1.09 (097–1.24)	1.53 (1.35–1.74)	

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Conclusion

Based on currently available data in the pediatric literature, we conclude there is compelling evidence to support the premise that a modest delay in appendectomy (e.g., the next calendar day for children presenting the night before) is a safe and reasonable practice. Although two studies (including one multicenter study) did show an increased risk of perforation with treatment delay, it is important to emphasize that none of the studies in this review demonstrated an increased risk for adverse events associated with measurable patient harm.

Although the data would suggest that treatment delay does not increase the risk of clinically relevant adverse outcomes within the first 24 hours, it is important to note that the influence of timely antibiotic administration was not addressed in many of the included studies. The role of antibiotics in arresting the progression of appendicitis has been well established in studies where antibiotics have been used as primary (and definitive) treatment for early appendicitis. It is plausible that antibiotics may also have played a role in mitigating the risk of perforation for the studies included in this review. Timely administration of antibiotics immediately following diagnosis should therefore be considered an essential part of any management strategy.

Finally, the relationship between TTA and resource utilization is complex and dependent on the outcomes examined. Longer TTA does not appear to be associated with hospital readmission, but does appear to be associated with increased cost and LOS, particularly in larger studies that include multiple hospitals with longer median TTAs. These results are perhaps not surprising; readmission encounters are often associated with adverse events such as organ space infections (of which there was no association with treatment delay), while longer delays to definitive treatment for any condition will likely lead to longer time in the hospital with increased charges associated with bed days and nursing shifts, among others. The ultimate decision surrounding timing of appendectomy in any hospital should balance the benefits of a timely intervention against the hospital's available resources.

Clinical Pearls

- A modest delay in appendectomy is acceptable; however antibiotics should be initiated in a timely fashion.
- Delay in appendectomy does not appear to significantly increase complications.
- Longer TTA is not associated with a higher readmission rate, but does correlate with an increased cost and length of stay.

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